Hodgkin’s Lymphoma

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NOTE: Consider Clinical Trials as treatment options for eligible patients.

DIAGNOSIS

- FNA alone is insufficient
- Hematopathology review of all slides with at least one tumor paraffin block. Rebiopsy if consult material is non-diagnostic.
- Core needle biopsy may be adequate if diagnostic, but an excisional \ nodal biopsy is recommended.
- Recommend staining for CD15, CD30, T and B panels, CD20, PAX5
- Adequate immunophenotype to confirm diagnosis
  - Paraffin panel for Hodgkin lymphoma (HL) including nodular lymphocyte predominant HL:
    - CD20, PAX-5, CD30, CD3, CD15, and CD45 (LCA)
    - EBER
- EBV proteins (i.e. LMP1) recommended for N.S. grade 2 or anaplastic variants

OF USE IN CERTAIN CIRCUMSTANCES

- Immunohistochemical studies:
  - LMP1
  - BOB1, OCT2, and CD79a (diff dx with B-cell lymphoma, unclassifiable with features intermediate between classical HL and DLBCL and primary mediastinal large B-cell Lymphoma).
  - CD21, CD23, or CD35 (follicular dendritic cell markers), CD57, BCL6 and IgD in cases of nodular lymphocyte predominant HL (may help with T-cell/hiostocyte rich large B-cell lymphoma)
  - CD2, CD43, ALK and EMA (diff dx with anaplastic large cell lymphoma)

STRONGLY RECOMMEND:

- Core biopsy for tissue banking by protocol

WORKUP

- History and physical including:
  - B symptoms (fever, sweats, weight loss)
  - ETOH intolerance
  - Pruritus
  - Fatigue
  - Performance status
  - Exam of nodes
  - Spleen, liver
- CBC, differential, platelets
- LDH, Liver Function Tests including: alkaline phosphatase, AST, ALT, and albumin, BUN, creatinine
- ESR
- Screening for HIV 1, HIV 2, hepatitis B and C (HBcAb, HBsAg, HCVAb)
- Chest X-ray
- CT Neck, chest, abdomen and pelvis
- PET/CT
- Bilateral bone marrow biopsies
- MUGA or echocardiogram
- Counseling: Fertility, psychosocial if clinically indicated

Useful in selected cases:

- Pregnancy test: women of childbearing potential
- Discuss fertility issues and sperm banking for patients of child bearing potential
- Semen cryopreservation, if chemotherapy or pelvic radiotherapy contemplated
- Cardiology consultation at baseline if risk factors for cardiac toxicity, i.e. obesity, abnl, echo, htn, hld

See Pages 2-3 for Clinical Presentations and Primary Treatment
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**Hodgkin’s Lymphoma**

**PRIMARY TREATMENT**

**Favorable** without any evidence of the following:
- Elevated Erythrocyte sedimentation rate greater than or equal to 50 mm/hour for stages I and IIA
- Elevated Erythrocyte sedimentation rate greater than or equal to 30 mm/hour for stages IB and IIB
- Nodal Regions greater than or equal to 3
- Extranodal Disease

**ABVD for 2 cycles and 20Gy of involved site radiation therapy**

**Unfavorable** with any evidence of the following:
- Elevated Erythrocyte sedimentation rate greater than or equal to 50 mm/hour for stages I and IIA
- Elevated Erythrocyte sedimentation rate greater than or equal to 30 mm/hour for stages IB and IIB
- Nodal Regions greater than or equal to 3
- Extranodal Disease

**ABVD for 4 cycles and 30Gy of involved site radiation therapy**

- **ABVD for 6 cycles and 30Gy of involved site radiation therapy**
- Or **Consider ABVD for 4 cycles and 30Gy of involved site radiation therapy**

See Page 4 for Response Assessment

---

**CLINICAL PRESENTATION**

**Classical Hodgkin’s Lymphoma**
- **Stage I-II, without Bulky disease**
- **Stage I-IIB, Bulky disease**

**ABVD**: Doxorubicin, bleomycin, vinblastine, dacarbazine

1. See Diagram 1 on page 7 for German Hodgkin’s Study Group (GHSG) Schematic of Nodal Sites
2. Extranodal disease, i.e. any tumor spread that involves other tissues than those of the lymph nodes, spleen, thymus, Waldeyer’s tonsillar ring, appendix and Peyer’s patches.
3. See Appendix A for Unfavorable Factors – Risk as defined by Hasenclever’s Model
4. See Appendix B for Radiation Therapy Guideline

---

**NOTE**: Consider Clinical Trials as treatment options for eligible patients.
## CLINICAL PRESENTATION

<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classic Hodgkin’s Disease</td>
<td>Advance Stages III, IV&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Lymphocyte Predominate Hodgkin’s Disease</td>
<td>Disease Stages, I, II</td>
</tr>
<tr>
<td>Lymphocyte Predominate Hodgkin’s Disease</td>
<td>Disease Stages, III, IV</td>
</tr>
</tbody>
</table>

## PRIMARY TREATMENT

- **ABVD**: Doxorubicin, bleomycin, vinblastine, dacarbazine
- **R-CHOP**: Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone
- **R-ABVD**: Rituximab, Doxorubicin, bleomycin, vinblastine, dacarbazine

1. **ABVD for 6 cycles with or without 30Gy of involved site radiation therapy**
2. **Involved site radiation therapy**
3. **Consider R-CHOP for 6 cycles**

### Advanced stage is consistent with an International Prognostic Score (IPS)

2. See Appendix B for Radiation Therapy Guideline

3. R-CHOP for 3-4 cycles followed by involved site XRT also an option

---

**NOTE:** Consider Clinical Trials as treatment options for eligible patients.

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**Page 3 of 13**

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Approved by the Executive Committee of the Medical Staff on 03/29/2016
Hodgkin’s Lymphoma

End of Therapy Response Assessment and Treatment of Classical Hodgkin’s and Lymphocyte Predominate Hodgkin’s

NOTE: Consider Clinical Trials as treatment options for eligible patients.

1 See Appendix C for Deauville Criteria
2 If biopsy positive, consider salvage treatment (See Appendix E for Chemotherapy Regimens). If biopsy negative, observation or consider radiation.

Department of Clinical Effectiveness V4
Approved by the Executive Committee of the Medical Staff on 03/29/2016
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Hodgkin’s Lymphoma

FOLLOW-UP AFTER COMPLETION OF TREATMENT

- Follow-up with an oncologist is recommended.
- Interim H&P: every 4 months for years 1 and 2 then every 6 months for years 3-5, then annually
- Pneumococcal and meningococcal revaccination every 6 years, if patient treated with splenic radiotherapy
- Annual influenza vaccine (especially if patient treated with bleomycin or chest radiotherapy)
- Laboratory studies:
  - CBC, platelets, Chemistry profile (LDH, Liver Function Tests including: alkaline phosphatase, AST, ALT, albumin, BUN and creatinine) every 4 months for years 1 and 2, then every 6 months for years 3-5, then annually
  - TSH every 6 months if radiotherapy to neck and optional for all other cases.
- CT chest/abdomen/pelvis 1 to 2 times during first year, then exam, chest x-ray, and labs for monitoring
- Annual breast screening: initiate alternating mammography and MRI 8 years post therapy or at age 35, whichever is sooner, if radiotherapy above diaphragm.
- Counseling: reproduction, health habits, psychosocial, cardiovascular, breast self-exam, skin cancer risk, end-of-treatment discussion.
- Recommend written follow-up instructions for the patient.
- Stress test/Echo for 10 year intervals after treatment is completed

NOTE: Consider Clinical Trials as treatment options for eligible patients.
Hodgkin’s Lymphoma

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**NOTE:** Consider Clinical Trials as treatment options for eligible patients.

**PATIENT PRESENTATION**

- Post-first-line therapy, chemotherapy alone or first-line therapy Combination: chemotherapy with radiotherapy
- Relapse or Refractory disease

**SALVAGE THERAPY**

- Complete response\(^1\) (CR)
  - Consider: ICE \(^1\), DHAP \(^1\), IGEV \(^2\), GND \(^2\)

- Partial response\(^1\) (PR)
  - Consider change to a different regimen\(^1\) including Brentuximab Vedotin

- Progressive disease post AHSCT?
  - Yes
    - Brentuximab Vedotin \(^3\), Clinical Trial

  - No
    - Monitor as clinically indicated (see page 5)

- Consider novel therapies on clinical protocols or gemcitabine-based chemotherapy regimens if not previously given

---

ICE: Ifosfamide, Carboplatin, and Etoposide
DHAP: High dose cytarabine, cisplatin and dexamethasone
IGEV: Ifosfamide, gemcitabine, vinorelbine and prednisone
GND: Gemcitabine, Navelbine and Doxil

\(^1\) See Appendix D for Response Criteria for Malignant Lymphoma
\(^2\) Biopsy if plan to treat with high-dose therapy
\(^3\) Conventional-dose chemotherapy may precede high-dose therapy. Sequence of therapy may vary. AHSCT = autologous hematopoetic stem cell transplant.

\(^4\) Extramedial disease, i.e. any tumor spread that involves other tissues than those of the lymph nodes, spleen, thymus, Waldeyer’s tonsillar ring, appendix and Peyer’s patches.

\(^5\) Selection of chemotherapy should be individualized.
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**APPENDIX A: UNFAVORABLE FACTORS**

<table>
<thead>
<tr>
<th>Unfavorable Factors</th>
<th>Unfavorable Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Localized Presentations</strong></td>
<td><strong>Advanced disease (International Prognostic Score)</strong></td>
</tr>
<tr>
<td>Bulky Mediastinal Mass</td>
<td>Albumin less than 4 g/dL</td>
</tr>
<tr>
<td>Elevated Erythrocyte sedimentation rate greater than or equal to 50 mm/hour for stages I and IIA</td>
<td>Hemoglobin less than 10.5 g/dL</td>
</tr>
<tr>
<td>Elevated Erythrocyte sedimentation rate greater than or equal to 30 mm/hour for stages IB and IIB</td>
<td>Male</td>
</tr>
<tr>
<td>Nodal Regions greater than or equal to 3</td>
<td>Age greater than or equal to 45 years</td>
</tr>
<tr>
<td>Extranodal Disease¹</td>
<td>Stage IV disease</td>
</tr>
</tbody>
</table>

¹ Extranodal disease, i.e. any tumor spread that involves other tissues than those of the lymph nodes, spleen, thymus, Waldeyer’s tonsillar ring, appendix and Peyer’s patches.

**Diagram 1:**
German Hodgkin’s Study Group (GHSG) Schematic of Nodal Sites

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**NOTE:** Consider Clinical Trials as treatment options for eligible patients.
Hodgkin’s Lymphoma

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### APPENDIX B: RADIATION THERAPY GUIDELINES

#### RADIATION THERAPY GUIDELINES

**Radiotherapy Alone Doses:**
- 30 Gy: Involved site
- Bulky lesions, greater than 5 cm = Consider 36 Gy: Involved site

**Combined Modality Radiotherapy Doses:**
- Stage I-II non bulky disease, favorable = 20 Gy: Involved site
- Stage I-II, non bulky disease, unfavorable = 30 Gy: Involved site
- Stage I-II, bulky, regardless of other risk factors = 30 Gy: Involved site

**Salvage Radiation Therapy Guidelines when Deauville greater than or equal to 4:**
- Involved site radiation to doses of 40-50 Gy

#### RADIATION FIELDS

Involved site: involved lymphoid region(s) only

### APPENDIX C: DEAUVILLE CRITERIA

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>no uptake</td>
</tr>
<tr>
<td>2</td>
<td>uptake less than or equal to mediastinum</td>
</tr>
<tr>
<td>3</td>
<td>uptake greater than mediastinum but less than or equal to liver</td>
</tr>
<tr>
<td>4</td>
<td>uptake greater than liver at any site</td>
</tr>
<tr>
<td>5</td>
<td>uptake greater than liver and new sites of disease</td>
</tr>
<tr>
<td>X</td>
<td>new areas of uptake unlikely to be related to lymphoma</td>
</tr>
</tbody>
</table>

A score of 1-3 was regarded as negative and 4 or 5 as positive.
Hodgkin’s Lymphoma

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APPENDIX D: RESPONSE CRITERIA FOR MALIGNANT LYMPHOMA

<table>
<thead>
<tr>
<th>Response Category</th>
<th>Nodal Masses</th>
<th>Spleen, Liver</th>
<th>Bone Marrow</th>
</tr>
</thead>
</table>
| **CR** (Complete Response: disappearance of all evidence of disease) | a. FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative  
b. Variably FDG-avid or PET negative; regression to normal size on CT | Not palpable, nodules disappeared | Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunohistochemistry should be negative |
| **PR** (Partial Response) | Greater than or equal to 50% decrease in SPD of up to 6 largest dominant masses; no increase in size of other nodes  
a. FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site  
b. Variably FDG-avid or PET negative; regression on CT | Greater than or equal to 50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen | Irrelevant if positive prior to therapy; cell type should be specified |
| **SD** (Stable disease: failure to attain CR/PR or PD) | a. FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET  
b. Variably FDG-avid or PET negative; no change in size of previous lesions on CT | Greater than or equal to 50% increase from nadir in the SPD of any previous lesions | New or recurrent involvement |
| **Relapse or Progressive disease** (Any new lesion or increase by greater than or equal to 50% of previously involved sites from nadir) | Appearance of a new lesion(s) greater than 1.5 cm in any axis, greater than or equal to 50% increase in SPD of more than one node, or greater than or equal to 50% increase in longest diameter of a previously identified node greater than 1 cm in short axis  
Lesions PET positive if FDG-avid lymphoma or PET positive prior to therapy | Greater than 50% increase from nadir in the SPD of any previous lesions |  |

FDG, \(^{18}\)F fluorodeoxy glucose  
SDP, sum of the product of the diameters

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Hodgkin’s Lymphoma

APPENDIX E: CHEMOTHERAPY REGIMENS FOR HODGKIN’S DISEASE

ABVD: Doxorubicin, bleomycin, vinblastine, and dacarbazine
ASHAP: Doxorubicin, methylprednisolone, high dose cytarabine, cisplatin
BEACOPP: Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone
CHOP: Cyclophosphamide, doxorubicin, vincristine, prednisone
CVPP: Cyclophosphamide, vincristine, procarbazine, prednisone
ICE: Ifosfamide, Carboplatin, and Etoposide
DHAP: High dose cytarabine, cisplatin and dexamethasone
IGEV: Ifosfamide, gemcitabine, vinorelbine and prednisone
GND: Gemcitabine, Navelbine and Doxil

NOTE: Consider Clinical Trials as treatment options for eligible patients.
Hodgkin’s Lymphoma

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SUGGESTED READINGS


Engert A, Diehl V, Pluetschow A, et al. (2009). Two cycles of ABVD followed by involved field radiotherapy with 20 gray (Gy) is the new standard of care in the treatment of patients with early-stage hodgkin lymphoma: final analysis of the randomized German Hodgkin study Group (GHSG) HD10. Study Supported by the Deutsche Krebshilfe and in Part by the Competence Network Malignant Lymphoma. Blood (ASH Annual Meeting Abstracts); 144:-716.


Suggested Readings Continued on Next Page
The International ChIVPP Treatment Group


Suggested Readings


Hodgkin’s Lymphoma

This practice guideline is based on majority expert opinion of the Lymphoma Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following medical oncologists, radiation oncologists, surgical oncologists, and hematopathologists:

- Bouthaina S. Dabaja, MD
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- Nathan Fowler, MD
- Fredrick Hagemeister, MD
- Larry W. Kwak, MD, Ph.D
- Sarah Milgrom, MD
- Loretta Nastoupil, MD
- Sattva Neelapu, MD
- Yasuhiro Oki, MD
- Chelsea Pinnix, MD, PhD
- Maria Alma Rodriguez, MD
- Jorge E. Romaguera, MD
- Felipe Samaniego, MD
- Grace Smith, MD, PhD
- Francesco Turturro, MD

Note: Consider Clinical Trials as treatment options for eligible patients.

DEVELOPMENT CREDITS

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